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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/740,653	12/18/2000	Chester A. Metcalf III	2003028-0008	4453

7590 09/24/2002

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EXAMINER	
BERCH, MARK L	

ART UNIT	PAPER NUMBER
1624	10

DATE MAILED: 09/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/740,653	METCALF ET AL.	
	Examiner	Art Unit	
	Mark L. Berch	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-195* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-27,54-59,61,88-90,94,97 and 107-195* is/are rejected.

7)☒ Claim(s) *28-53,60,62-87,91-93,95,96 and 98-106* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claim Objections

Claims 28-53, 60, 62-87, 91-93, 95-96, and 98-106 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. Thus, all multiply dependent claims which depend on e.g. claim 19 are improperly multiply dependent. See MPEP § 608.01(n) ("a multiple dependent claim may not serve as a basis for any other multiple dependent claim, either directly or indirectly."). Accordingly, claims 28-53, 60, 62-87, 91-93, 95-96, and 98-106 have not been further treated on the merits.

The requirement for election of species is withdrawn.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-5, 7, 12-17, 107, 112, 114, 116, 122-124, 175-178, 180, 182-183 are rejected under 35 U.S.C. 102(b) as being anticipated by Dang.

In columns 19-28, see species 18-26, 47-54, 192-193, 260-266.

The bone treatment claims are included because diabetes is well known as a cause for Osteomyelitis, a bone infection.

Claims 1-3, 6-7, 9, 14, 16, 111, are rejected under 35 U.S.C. 102(b) as being anticipated by Kondo.

See compound 4b.

Claims 1-5, 7, 9, 14, 16, are rejected under 35 U.S.C. 102(b) as being anticipated by Filipov, Tate, Wada.

In Filipov, see 5 and 6. In Tate, see 1 and 9. In Wada, see all the products formed in scheme 2. In Charubala, see 6.

Claims 1-5, 7, 9, 14, 16, 18, 54, 112, 114, 117, 122-123, and 175 are rejected under 35 U.S.C. 102(b) as being anticipated by Brush.

See the product formed in Figure 1B. Claim 18 is rejected because of the aryl rings at the top of the structure.

Claims 1-5, 7, 9, 14, 17-18, 112, 114, 116-117, 121-123, 175 are rejected under 35 U.S.C. 102(b, e) as being anticipated by Suhadolnik.

Note the PCT publication date of 12/17/1998. See columns 4-5, and note that Ade^{Bn} and Ade^{Bz} meet the requirement for the claims. Compounds 22-25 have two P groups and hence avoid the proviso. The reference also teaches additional diphosphate and triphosphate derivatives prepared in example 8. With regard to e.g. claim 17, $Base^{1}$ would qualify as the heteroaryl.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 10 is rejected under 35 U.S.C. 103(a) as being unpatentable over Dang.

Note the anticipation rejection above. This claim calls for an amino substituent at the 2-position. This is taught in the definition of E (see last choice). Although the indicated species do not have this, other species i.e. 168-171, do have such a feature, so it is taught as an obvious variation.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-27, 54-59, 61, 88-90, 94, 97, 107-195 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. The term "aliphatic" has been rendered indefinite by the specification. Aliphatic means lacking in rings. But page 11, line 6 says that aliphatic includes things with

cycles, and cycloalkyl is listed; others appear at page 22, lines 18-20 etc. While applicant may be his or her own lexicographer, a term in a claim may not be given a meaning repugnant to the usual meaning of that term. See *In re Hill*, 161 F.2d 367, 73 USPQ 482 (CCPA 1947). Since applicants have obliterated the essential requirement for aliphatic, there is no way of knowing what the term means to exclude, since it appears to cover everything. Thus, e.g. claim 54's or claim 108's "cyclic ... aliphatic" is self-contradictory and meaningless. For purposes of interpreting the proviso in claim 1, the term is understood in its full breadth as given in the specification.

2. Further the phase "aliphatic, heteroaliphatic" appears to be redundant, since the former completely embraces the latter.
3. Likewise, the term "substituted or unsubstituted aliphatic" (e.g. at page 125, lines 5-6) makes no sense, as aliphatic already permits substituents.
4. Similarly, it is unclear what "heteroaliphatic" means either. It appears to be any moiety which has an atom other than C and H. Is that what is intended?
5. The text at page 123 lines 18-21 "wherein ... unsubstituted" is of unclear purpose. This appears to repeat what the specification already says, and hence, if it were to be removed, the scope of the claim would be the same. Hence, its function is unknown.
6. It is unknown what "terminal functionality representing a cyano" at page 123, line 24 refers to. Cyano is self terminating, as it can take no further substituent. Thus, would CH(CN)Ethyl be terminated with CN, and the ethyl is just a substituent on the cyano-methyl? Or is it not terminated, as the ethyl continues the chain? What exactly is a "terminal functionality"?

7. X being alkyl (e.g. last line of page 124 and many other places) is impossible, as it would give a P atom with 4 bonds and no charge. This should be removed from the specification as well.
8. The term "or pharmaceutically acceptable derivative" (e.g. end of claim 2) is of unknown scope. What is a derivative? What level of change can be made in the compounds and it still be a derivative? Can the P be removed?
9. Further, claim 1 makes no provision for such derivatives, so claim 2 is improperly dependent on claim 1.
10. The term "comprising" in the first line of claim 1 renders the claim open-ended; deletion is suggested.
11. The term "alkylaryl" at page 123, lines 12, 13 and 14 appears superfluous, since aryl is already permitted to have any kind of substituent.
12. Likewise for "alkylheteroaryl".
13. The 3rd, 4th, and 5th structures of page 124, line 15 (and elsewhere) are clearly in error. The bond to the M would mean that the O or S would have three bonds, the N would have 4 bonds, or the C would have 5 bonds. Bonding must be to an atom with a free valence, as is seen in all the other choices. A trivalent choice (see e.g. the variable L) needs to be used.
14. The last choice for Y at e.g. page 124, lines 10 and 19 is clearly in error, since this would give a four bonded N with no charge. Was $C(R_J)_2$ or $N(R_J)$ intended? For whichever choice is made, applicants must show that one of ordinary skill in the art would have known that this choice, and not another, was intended.

15. Claim 7's "additionally substituted with 0-3 substituents" makes no sense. If the number is zero, then it is not additionally substituted.

16. "Amido" is indefinite (e.g. page 125, line 21). There is no way of knowing whether applicants intend just carboxylic acid amides, or whether sulfonic, phosphonic, etc amides are intended. But even if carboxylic acid amido is intended, the term is undefined. Such a molecule generically has the formula RC(O)NR'R". One of the R choices will be used to attach, depending on whether the amido is C- or N-bound. Which end is intended for attachment? What is the nature of the other two R groups? Can the two of them together form a ring, and if so, of what type?

17. The choices of "ketone" and "aldehyde" as substituents are impossible. These are molecules (e.g. acetone) and as such have no valence with which to attach.

18. The scope of claim 182 is unclear. Is this the amount per administration? Per day? Per month? Per course of treatment? Lifetime dosage?

19. The term "acyl" (e.g. page 125, line 21) is indefinite. Does this embrace acids of S? P? As? What does the stem look like, i.e. if the acyl is e.g. RC(O), what is R?

20. Sulfonyl at page 125, line 22 (and page 126, line 19, etc.) makes no sense. Sulfonyl is the divalent $-SO_2-$ radical, but is used for a monovalent moiety. Likewise sulfoxido (i.e. -S(O)-), sulfonate and sulfonamido (which can be divalent, $-SO_2NH-$ or trivalent, $-SO_2N<$, depending on how it is understood, which is not clear).

21. Likewise "sulfate" on the same line is trivalent.

22. The intended scope of "Phosphorous containing moiety" is unclear. Could this include a cationic substituent which had a phosphate anion as a counterion, or an anionic substituent (e.g. carboxylate) with a phosphonium cation as a counterion?

Would it include P atoms without functional groups, such as $-PO_2$ or phosphazene rings? Would it include highly reactive groups such as $-PCl_2$? The specification discussion is completely open-ended and does not discuss these issues.

23. The last two claim 140 choices are not alkyl, but cycloalkyl, so that the claim is improperly dependent on claim 139.

24. "Prodrug thereof" in claim 2, 20, etc. is indefinite. Determining whether a given derivative definitely is or is not a prodrug involves more than routine experimentation. If the derivative is active, open-ended experimentation may be involved to determine for sure whether the compound is a prodrug or whether it is active in its own right.

25. What role does the word "scaffold" have at page 123, line 27. How would the claim differ if the word were removed?

26. In "protected forms" (e.g. at page 127, line8) protecting against what? These are final products, so what is there to protect against? As there is no such thing as a universal protecting group, correct selection of a protecting group requires some knowledge of what is being protected against.

27. The last choice of page 127, line 7, is superfluous, as it is already covered by the previous term. Likewise in claim 21, etc.

28. Likewise, the "lower alkyl, lower alkenyl" of page 126, lines 17-18 is already covered by the last term on page 126 and the first term on page 127. Likewise in claim 21, etc.

29. The last line of claim 122 is of unknown purpose. OH is already a permitted substituent, so that if those "optionally substituted" claim language were removed, the scope would still be the same. Likewise claim 121, 135, etc.

30. The term "thio" as a substituent (e.g. last line of claim 134)is a generic one, indicating the presence of sulfur in some form. Properly used, it is only a prefix, referring to the replacement of O with S. As a substituent, it has no one single generally accepted meaning. There could be intended thioxo (=S) or mercapto (-SH). If it denotes replacement by S of some other atom as in "thioalkoxy", then the rest of the term is missing; was "thioalkoxy" intended? Perhaps some other term which began with "thio", like thiophene was intended. Whatever choice is selected must be supported by the specification.

31. Claim 138 is improperly dependent on claim 137 when n is not zero. There are not amino groups, but amino-alkyl group.

32. Claims 139-143 are all improperly dependent on claim 138. For example, claim 140 has R_C = e.g. methylamino, not permitted by claim 137. Claim 142 has e.g. pyridylamino, not permitted by claim 138. Note that claim 138 requires that there be two N atoms present, neither of which is present in a ring.

33. The variable HA is not defined in claim 158. There is a reference to when its absent, but the variable itself is not defined.

34. What exactly is a "bone-related disorder" --- that is, how is it different from the "bone disorder" of claim 180? It would appear to cover joints as well, but what else?

35. The expression "one of more" at claim 18, line 2 is unclear.

36. Claim 88's first "whereby" is not clear. If RC is e.g. aryl, then this condition cannot be met, since neither RE nor RF even exist. Thus, it is not apparent why the first 4 choices for RC are even listed.

37. The same sort of problem exists in claim 107.

38. Claim 116 cannot depend on claim 112, as R1 does not exist in claim 112.

Claims 7-18, 21, 26, 90, 114, 129, 178-179 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

A. If sulfate is not intended as the trivalent choice (see point 21 above) but instead the monovalent $-SO_3^=$ substituent, then this will produce a charged compound with a net charge of –2, as no cation is provided. Such is impossible.

B. The "carbonyl" and "thiocarbonyl" choices, i.e. =C=O and =C=S will produce a ketene or a thioketene. These are too reactive to function in pharmaceuticals.

Claims 176-183 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Prevention and treatment of bone disorders generally is not enabled. If claim 183 were limited to dependence on claim 176, it would be allowable.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state

of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims.

(a) Scope of the compounds. There are four substituents present on the purine nucleus, and each is defined extremely broadly. The genus thus easily covers trillions of compounds.

(b) Scope of the diseases covered. The scope of bone disorders is immense. The term includes common bone disorders such as Paget's disease, hereditary multiple exostosis, and osteoporosis. It also includes Dysplasias including Osteogenesis imperfecta, Osteopoikilosis, Osteopetrosis (Albers-Schoenberg disease), achondroplasia, Osteochondromatosis, Caffey's disease, Lenz-Majewski syndrome, Melorheostosis, metaphyseal dysplasia (Pyle disease), pyknodysostosis, sclerosing diaphyseal dysplasia (Camurati-Engelmann Disease), spondyloepiphyseal dysplasia and many others. It includes dense bones disorders, including axial osteomalacia, fibrogenesis imperfecta ossium, sarcoidosis and tuberous scelrosis. Other bone disorders include cleidocranial dysostosis, coxa plana, Hand-Schueller-Christian disease, brachydactyly, calcium pyrophosphate deposition disease (CPPD), Wormian bones, tibia vara (Blount disease), cervical spine fusion (ankylosis), Crouzon syndrome,

slipped capital femoral epiphysis (SCFE), celery-stalk metaphyses, Bankart deformity, Ollier disease, craniosynostosis, Erlenmeyer flask deformity, ivory vertebral body, spheroid calcification, acro-osteolysis, Caffey disease, cherubism, Sever disease, Sprengel deformity, Panner disease, osteogenesis imperfecta, Letterer-Siwe disease, Pott's disease, Scheuermann disease, sabre-shin deformity, basilar invagination, degenerative disc disease, block vertebra, Kohler disease, hyperostosis frontalis interna, diastrophic dwarfism, osteochondrosis, posterior vertebral scalloping, multicentric reticulohistiocytosis, osteitis fibrosa, vertebra plana, Hill-Sachs deformity, Kienbock disease, spontaneous osteolysis and many, many more. Included also are bone tumors, including Osteosarcomas (osteoblastic, chondroblastic, fibroblastic, telangiectatic and others), Hemangiosarcoma, Periosteal chondrosarcoma, Periosteal fibrosarcoma, Maxillary fibrosarcoma, Parosteal osteosarcoma, Periosteal osteosarcoma, Malignant mesenchymoma, Liposarcoma, synovial sarcoma, Osteochondroma, Hemangioma, Myxoma of the jaw, Ossifying fibroma, Osteoma, Giant cell tumor of bone, multiple myeloma, solitary myeloma, reticulum cell sarcoma, malignant fibrous histiocytoma, desmoblastic fibroma of the bone, periosteal fibroma, lipoma, Hemangioendothelial sarcoma, Ewing's sarcoma, chondroblastoma, and Multilobular tumor of bone. There are also tumor-like lesions, including osteoid Osteoma, non-osteogenic Fibroma, benign osteoblastoma, Solitary bone cyst, Juxtacortical bone cyst, Myositis ossificans, Villonodular synovitis and Epidermoid cyst of the phalanx. There are also secondary malignant deposits in bone.

(2) The nature of the invention and predictability in the art: The invention is directed toward the treatment of disease and is therefore physiological in nature. It is well

established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance: That provided is very limited. The dosage range information given in the sentence bridging pages 50-51 is not associated with any particular disease. Only a few bone diseases are mentioned specifically.

(4) State of the Prior Art: One skilled in the art knows that bone disorders can arise from a huge assortment of unrelated causes. These include Ehlers-Danlos syndrome, galactosemia, cirrhosis, vitamin D malabsorption arising from GI disorders such as celiac disease, from pancreatic insufficiency, from biliary atresia and other sources; abnormal vitamin D metabolism arising from e.g. anticonvulsant therapy, chronic renal failure, etc.; hyperparathyroidism and hypoparathyroidism and pseudohypoparathyroidism; Marfan syndrome, fluorosis (excessive fluoride intake), ochronosis, lead poisoning, cadmium poisoning, Morquio's disease, Cushing's disease, Gaucher disease, tyrosinemia, homocystinuria, scurvy, ToRCHS syndrome, renal osteodystrophy, Hypertrophic osteoarthropathy, Klippel-Feil syndrome, sickle cell anemia, glycogen storage disease, Niemann-Pick disease, hyperuricemia, renal transplantation, hemophilia, gout, histiocytosis X, Tuberculosis, hypervitaminosis A and D, frostbite, burns, leprosy, polyvinylchloride exposure, progeria, acromegaly, basal cell nevus syndrome, Erdheim-Chester disease, psoriasis, Ligna-Franconi Diseasesteroids, shoulder dislocation, juvenile rheumatoid arthritis, Wilson's Disease, hypophosphatasia and pseudo hypophosphatasia, ingestion of phosphate binding

antacids, and of mineralization inhibitors such as Etidronate, dietary deficiencies in phosphate and calcium, brain tumors, alcohol abuse, bone fracture, diabetes, caisson disease, irradiation, hemodialysis, hepatitis C, milk-alkali syndrome, carbonic anhydrase II deficiency and many, many more. The secondary malignant deposits in bone arise from primary malignancies in the thyroid, breast, bronchus, kidney and prostate. There are a wide assortment of genetic problems, many of them poorly understood, which cause bone disorders. And often, the cause is unknown. For example, Paget's disease is the second most common disorder of the bone, and its origin is unknown.

(5) Working Examples: There are no working examples for the treatment of any disorder. Assorted tests are mentioned, but no data is provided for any specific compounds.

(6) Skill of those in the art: The skill level varies greatly according to which disorder is involved. For e.g. osteoporosis the skill level is good. For many others, the skill level is extremely low, as there have been no successful pharmacological treatments. An example is the assorted osteosarcomas; no chemotherapy has even been demonstrated as a successful mode. Further, the skill level for prevention, which is mentioned in claims 180-181, is lower still. Even some which can be treated, e.g. Paget's, cannot be prevented from occurring in the first place.

(7) The quantity of experimentation needed: In view of the extreme diversity of such disorders, the extreme breadth of the genus of compounds, the known difficulty of treating bone disorders with medicinals, the level of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Claims 184-195 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

These claims call for the treatment of cancer and tumors generally.

Pursuant to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), one considers the following factors to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. Some experimentation is not fatal; the issue is whether the amount of experimentation is "undue"; see *In re Vaeck*, 20 USPQ2d 1438, 1444.

The analysis is as follows:

(1) Breadth of claims.

(a) Scope of the compounds. There are four substituents present on the purine nucleus, and each is defined extremely broadly. The genus thus easily covers trillions of compounds.

(b) Scope of the diseases covered. The coverage is immense. There are hundreds of types of cancers and tumors. They can occur in pretty much every part of the body.

(2) The nature of the invention and predictability in the art: The invention is directed toward medicine and is therefore physiological in nature. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(3) Direction or Guidance: That provided is very limited. The dosage range information given in the sentence bridging pages 50-51 is not associated with any particular disease. No specific cancers are named in the specification.

(4) State of the Prior Art: The prior art knows that there never has been a compound capable of treating cancer generally. There are compounds that treat a modest range of cancers, but no one has ever been able to figure out how to get a compound to be effective against cancer generally, or even a majority of cancers. Thus, the existence of such a "silver bullet" is contrary to our present understanding in oncology. Even the most broadly effective antitumor agents are only effective against a small fraction of the vast number of different cancers known. This is true in part because cancers arise from a wide variety of sources, such as viruses (e.g. EBV, HHV-8, and HTLV-1), exposure to chemicals such as tobacco tars, genetic disorders, ionizing radiation, and a wide variety

of failures of the body's cell growth regulatory mechanisms. Different types of cancers affect different organs and have different methods of growth and harm to the body, and different vulnerabilities. In addition, note that these compounds are adenine derivatives. So far as the examiner is aware, adenines have never been used to treat cancer.

(5) Working Examples: There are no working examples for the treatment of any disorder. Assorted tests are mentioned, but no data is provided for any specific compounds.

(6) Skill of those in the art: It is beyond the skill of oncologists today to get an agent to be effective against cancers generally, evidence that the level of skill in this art is low relative to the difficulty of such a task. The skill thus depends on the particular cancer involved. There are cancers where the skill level is high and there are multiple successful chemotherapeutic treatments. In many, many cancers, however, there is no chemotherapy whatsoever available.

(7) The quantity of experimentation needed: In view of the extreme diversity of such disorders, the extreme breadth of the genus of compounds, the known difficulty of getting anti-cancer compounds to actually work, the level of experimentation is expected to be high.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*,

999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here.

Information Disclosure Statement

And IDS was filed, but either the references were not enclosed or the PTO has lost the documents. A replacement set will be needed.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-27, 54-59, 61, 88-90, 94, 97, 107-195 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-18, 35-39 of copending Application No. 09/740393. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the two cases are broadly overlapping.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Specification

The abstract is objected to as too vague.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Berch whose telephone number is 703-308-4718. The examiner can normally be reached on M-F 7:15 - 3:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 708-308-1235.

Mark L. Berch
Primary Examiner
Art Unit 1624

September 20, 2002